

EXHIBIT 12

COWEN

EQUITY RESEARCH

April 6, 2021

■ Biotechnology

INDUSTRY UPDATE

FAILED EXPAREL STUDIES OPEN THE DOOR TO AN EFFECTIVE HTX-011 MARKETING CAMPAIGN

THE COWEN INSIGHT

Heron's PDUFA (5/12/2021) for HTX-011 is the first meaningful challenge to Pacira's Exparel in postsurgical pain management. Despite the regulatory risk, we believe that Heron has multiple advantages in strength of efficacy data and convenience of administration. A number of negative studies recently published and soon to report could be effectively used to counter-market against Exparel.

HTX-011 the First Meaningful Challenger to Exparel

Heron's upcoming PDUFA date for HTX-011 (5/12/2021) is the first time we could see a meaningful competitor into the postsurgical pain management space to challenge Exparel. Xaracoll and Posimir were approved with limited labels due to weak efficacy data that we expect will prevent them from becoming substantial competitors to Exparel. However, we anticipate HTX-011 to be approved with a broad label similar to Exparel but with stronger clinical data due to the use of an active comparator in the registrational trials.

Potential Upside from Regulatory Risk for HTX-011

Investors see significant risk for HTX-011's approvability. HTX-011 received 2 CRLs (for non-clinical issues) and the FDA DAAP group has a history of missing PDUFA dates and surprise CRLs. This risk is being reflected in the short interest in HRTX, which has been rising over the last 6 months. We see a large potential upside with the approval of HTX-011 (100%+).

Failed Exparel Studies Create an Opportunity for HTX-011 Marketing

A key investor question has been whether Heron will be able to effectively market HTX-011 if approved since Exparel is viewed as an entrenched market leader. Multiple recent publications have cast doubt on the efficacy of Exparel, especially vs active comparators (recall Exparel was approved in studies vs placebo, but standard of care is generic bupivacaine). There are 88 additional trials in progress testing Exparel in a variety of indications that have potential negative readouts. These studies are not presently receiving much attention, but could be used to effectively counter-market if HTX-011 is approved.

Pacira Model Updated to Reflect Slower Growth Rate Post HTX-011

We updated our Pacira model to reflect a decrease in the rate of Exparel growth after 2021 due to sales pressure from approval of HTX-011. We now model Exparel sales growing to \$611M in 2026, below consensus of \$776M.

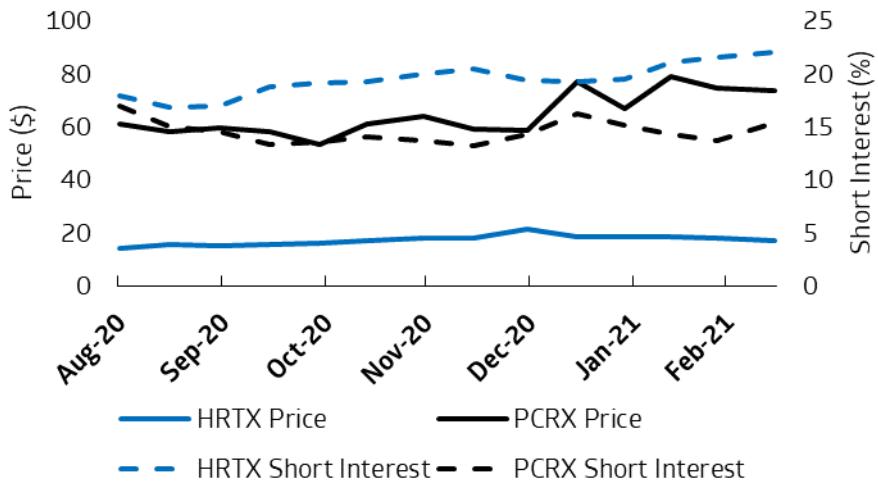


EXparel: THE NUMBNESS IS WEARING OFF

Pacira's Exparel (liposomal bupivacaine) is the clear market leader in branded post-surgical local anesthesia. Recent entrants into this market – Innocalls's Xaracoll (bioresorbable collagen embedded bupivacaine) and Posimir's Durect (polymer based bupivacaine) – have been unable to effectively compete due to their limited labels. However, we believe that Exparel's success rests on an unstable foundation. The three studies that initially led to Exparel's approval in 2011 compared Exparel to placebo, not the standard of care (SOC) – generic bupivacaine. Pacira did complete a Phase 4 post-marketing study in which they compared Exparel to bupivacaine, but statistical and methodological issues have raised doubts about the clinical applicability of these findings. Despite those issues, Exparel has propelled Pacira to revenues >\$400MM. Heron's HTX-011 is a polymer-based bupivacaine that has shown clear benefit over SOC in head-to-head trials but has received 2 CRLs in the past 2 years for non-clinical issues. HTX-011's upcoming May 12, 2021 PDUFA target date sets the stage for a market competition between these two compounds if HTX-011 is approved, as we expect.

A key question we have been receiving from investors leading up to the HTX-011 PDUFA is – if approved, will Heron be able to effectively market HTX-011 vs Exparel? Based on the trials for both drugs, we expect the answer is yes – we believe HTX-011 will be able to compete both on efficacy, safety, and convenience. Furthermore, a recent series of journal publications of investigator-sponsored trials (ISTs) comparing Exparel to bupivacaine has begun to cast further doubt on Exparel's ability to beat SOC broadly. Due to the fact that Xaracoll and Durect have been ineffective competitors to Exparel, we suspect there has been little effort dedicated to marketing these negative results. These data are likely to become more significant if and when HTX-011 is approved, since the Phase 3 trial of HTX-011 included bupivacaine as an active comparator.

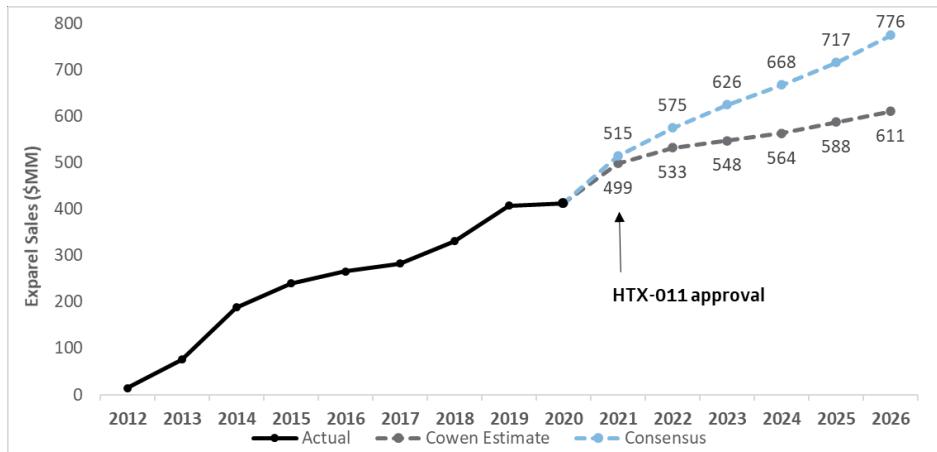
Nevertheless, the approval of HTX-011 isn't without controversy. After 2 CRLs there is a contingent of investors who have significant doubts about its overall approvability. We believe that the approval of HTX-011 in Europe in 2020 bodes well for its approvability in the US. We expect HTX-011 to be approved and model peak sales of \$1.3B in 2035. Short interest in HRTX (shown below) has been building, suggesting large potential upside with HTX-011 approval. In the rest of this report, we briefly review the data supporting Exparel's label and look at the emerging body of literature directly comparing Exparel with SOC. These data are likely to form the basis of an effective marketing strategy by Heron post-approval.

**Short Interest in HRTX Building Since August 2020**

Source: Cowen and Company, Thomson Reuters

Exparel: Leading the Market with a Broad Label

Exparel, Xaracoll, and Posimir are the only approved extended-release bupivacaine for post-operative pain indications. Exparel was approved in 2011 and carries label indications for post-surgical local analgesia via infiltration and interscalene brachial plexus nerve block for post-surgical regional analgesia. Xaracoll was approved in August 2020 and its label indication is for 24 hours of post-surgical analgesia only after open inguinal hernia repair. Posimir was approved in February 2021 and its only label indication is for 72 hours of post-surgical analgesia after arthroscopic subacromial decompression. We do not see either of these as significant threats to Exparel's market leadership. Pacira reported 2020 Exparel sales of \$413M and we project sales growing to \$611M in 2026, below consensus estimate of \$776M.

Exparel Annual Sales, Actual and Projected, 2012-2026

Source: Cowen and Company, Consensus from Thomson Reuters

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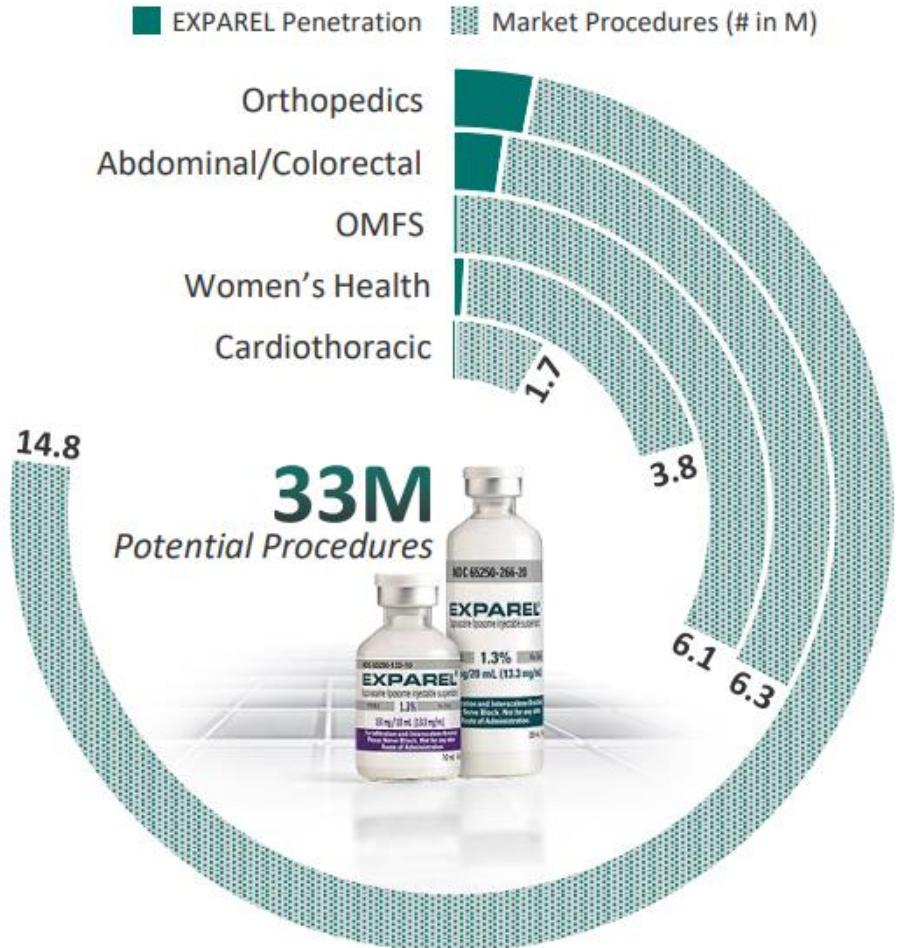
We anticipate the 2021 approval of HTX-011 will affect the growth trajectory of Exparel. We also want to be clear that we don't anticipate HTX-011 will shrink Exparel's market, but we do anticipate it to have a material impact on future growth. Therefore our projected rate of Exparel growth is below consensus in 2022 and beyond. We believe Heron will be more effective at marketing into new segments and potentially incrementally taking share from Exparel. We remain Market Perform on Pacira.

Exparel's Approval Left Something to be Desired

Exparel's approval for the local analgesia indication was supported by a bunionectomy study and a hemorrhoidectomy study. The bunionectomy study randomized 193 patients to Exparel or placebo. There was a reduction in pain through 24 hours as measured by the AUC of the numerical rating scale (NRS), but there was no difference in morphine equivalents used through 24 hours, and there was not a statistically significant difference in the number of patients using ketorolac. The hemorrhoidectomy study randomized 189 patients to Exparel or placebo. Again AUC of the NRS scores was significantly reduced in the Exparel group, and the differences between the groups were most evident in the first 24 hours. Additionally, 28% of patients in the Exparel group required no rescue pain medication vs 10% in the placebo, and the mean amount of morphine used over 72 hours was 22 mg in the Exparel group but 29 mg in the placebo group. This difference was statistically significant but even the label questions whether this difference is clinically meaningful.

Our consultants and KOLs have repeatedly raised the issue of placebo comparator in these trials. The standard of care for local analgesia is not placebo – it is an active drug. Surgeons commonly use one or a mixture of generic bupivacaine, ropivacaine, lidocaine, and procaine for this purpose. Given that the cost of Exparel is nearly 100x the cost of generic bupivacaine, physicians want to see data for Exparel against active comparator instead of placebo. Pacira performed a post-marketing study (the PILLAR trial) with the goal of addressing this concern. In PILLAR, the Exparel arm achieved a statistically significant reduction in AUC of visual rating scores (VRS) vs control ($p=0.0381$). Patients who received Exparel consumed significantly fewer opioids versus control during the 48 hours that followed surgery ($p=0.0048$). Additionally, a higher fraction of patients on Exparel required no rescue medication ($p = 0.023$), although the absolute delta between the two curves is rather modest. The study design left some unanswered questions. Primarily, the two arms were bupivacaine and Exparel + bupivacaine, and in the Exparel + bupivacaine arm the patients received more total bupivacaine than in the SOC comparator. As such, the trial was not a head to head vs. SOC, but an add-on of Exparel to bupivacaine.

Market Penetration of Exparel

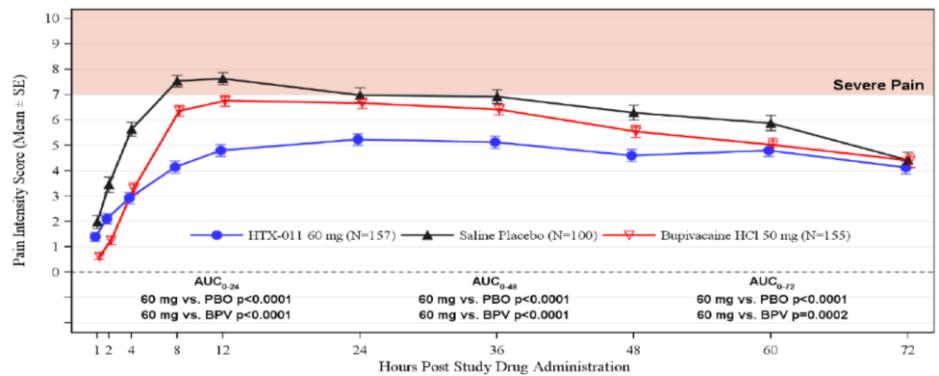


Source: Pacira

HTX-011's Registrational Trials Include an Active Comparator

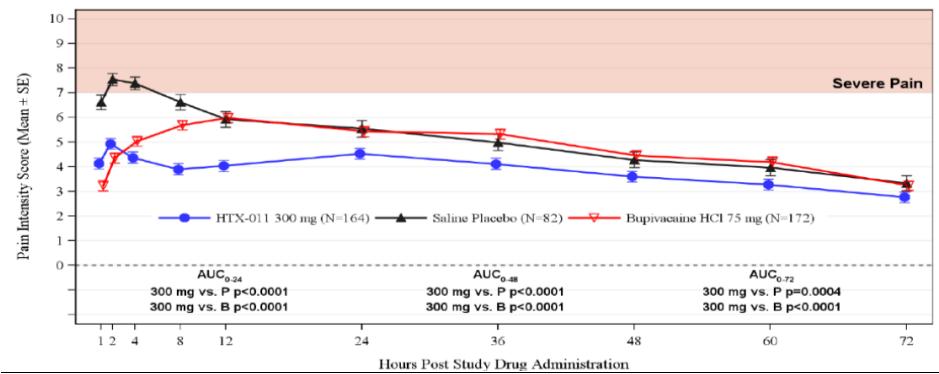
Heron studied HTX-011 in multiple trials that included an active comparator. Study 301/EPOCH1 was a Phase 3 bunionectomy trial that compared instilled HTX-011 vs generic bupivacaine vs placebo and showed a significant reduction in pain intensity scores over a 72 hour period after surgery. Although we don't anticipate an opioid-sparing claim on the label, there was also a significant increase in patients remaining opioid free through 72 hours (53.5% vs 75.5% in bupivacaine group, p<0.0001).

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HTX-011 Study 301/EPOCH1 Bunionectomy Pain Intensity Scores

Source: Heron Therapeutics

Study 302/EPOCH2 was a Phase 3 herniorrhaphy trial that compared instilled HTX-011 vs generic bupivacaine vs placebo and the results were similar to study 301. There was a significant reduction in pain intensity scores through 72 hours and fewer patients requiring opioids (48.8% vs 60.5% in bupivacaine group, p=0.0372).

HTX-011 Study 302/EPOCH2 Herniorrhaphy Pain Intensity Scores

Source: Heron Therapeutics

Emerging Data Casts Doubt on Exparel's Efficacy vs SOC

Since Exparel's approval in 2011, there has only been one voice in the room: Pacira. That has helped lead to the impressive growth of Exparel sales. As of March 2021, Pacira was estimating a total addressable procedure market of 33M procedures. Based on the published WAC for Exparel and reported Exparel sales, we estimate Pacira has captured ~1.5M or 4.5% of these procedures. However, we heard from many physicians the desire to see real head-to-head data for Exparel vs. bupivacaine, and Pacira refused to conduct such trials. As such, independent investigators decided to address this question across a variety of surgical settings.

A significant body of literature from independent investigators has accumulated over the last several years that has begun to cast doubt on the effectiveness of Exparel. Most of these studies are ISTs (investigator sponsored trials) that don't receive much press. The February 2021 edition of *Anesthesiology* featured two articles on Exparel – one a

narrative review, the other a systematic review and meta-analysis. Both of these articles concluded that there is insufficient benefit of Exparel to justify the costs.

The narrative review, published by Ilfeld et al, summarized results from 76 trials of Exparel across a wide range of procedures (no procedures were excluded). For infiltrative local analgesia, there were 12 trials vs placebo; 7 of 12 failed to find a benefit of Exparel on pain scores, opioid consumption, or length of hospital stay. In the 5 that did find a benefit, the overall risk of bias was high (judged by the Cochrane Risk of Bias tool). There were 36 trials with an active control arm. Of the 19 non-TKA studies, 15 failed to find a difference for all outcome variables at all time points. In the 4 of 19 that had a difference, 3 had a high bias. Even in the studies with positive results, they were deemed clinically insignificant due to magnitude of effect being small or being time-limited. In TKA studies, 15 of 17 failed to find an effect on the primary outcome. Results for nerve block indications were similar. In 12 active-controlled RCTs, only 6 found a clearly statistically significant benefit of Exparel on any outcome.

The systematic review and meta-analysis by Hussain et. al. evaluated Exparel vs unencapsulated bupivacaine in peripheral nerve blocks. The primary endpoint was the 24 hours to 72 hours difference in weighted mean AUC of pain scores. There were 9 trials included. The difference between Exparel and bupivacaine was statistically significant (1 cm/hour, p=0.0003) in favor of Exparel but was judged to be clinically insignificant with investigators assigning 2 cm/hour as minimally clinically significant benefit. However, we would like to point out that Heron has no near-term plans to expand HTX-011 label to nerve block, so these studies are less significant from the competitive perspective.

Additional studies have been published and are underway that bolster this conclusion. An RCT (randomized control trial) comparing Exparel to bupivacaine published in the *Canadian Journal of Anesthesiology* in January 2021 showed no improvement with Exparel in TAP blocks for open hysterectomy in time to first opioid use or total opioid consumption in 72 hours. Another RCT published in the *American Journal of Obstetrics & Gynecology* published in January 2021 showed no benefit to Exparel when added to unencapsulated bupivacaine after ex-lap for gynecologic indications; primary outcome was percent of patients opioid free at 48 hours. Yet another RCT published in *JAMA Network Open* in March 2021 randomized patients with truncal incisions to Exparel or unencapsulated bupivacaine and found that neither pain scores nor opioid use was different between the two groups.

Recent Articles on Exparel

Author	Title	Journal Reference	Description
Ilfeld et al	Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain	Anesthesiology 2021; 134:282-344	Narrative review of 76 trials.
Hussain et al	Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia	Anesthesiology 2021; 134:147-64	Systematic review and meta-analysis of 9 peripheral nerve block trials.
Fidkowski et al	A randomized-controlled trial comparing liposomal bupivacaine, plain bupivacaine, and the mixture of liposomal bupivacaine and plain bupivacaine in transversus abdominus plane block for postoperative analgesia for open abdominal hysterectomies	Canadian Journal of Anesthesiology 2021 https://doi.org/10.1007/s12630-020-01911-1	Exparel vs bupivacaine in TAP block.
Meyer et al	A prospective randomized trial comparing liposomal bupivacaine vs standard bupivacaine wound infiltration in open gynecologic surgery on an enhanced recovery pathway	Am J Obstet Gynecol 2021;224:70.e1-11	Exparel vs bupivacaine after laparotomy (infiltration).
Sandhu et al	Effectiveness of Standard Local Anesthetic Bupivacaine and Liposomal Bupivacaine for Postoperative Pain Control in Patients Undergoing Truncal Incisions	JAMA Network Open. 2021;4(3):e210753. doi:10.1001/jamanetworkopen.2021.0753	Exparel vs bupivacaine with truncal incisions (infiltration).

Source: Cowen and Company

Results like this are likely to keep coming in. According to ClinicalTrials.gov there are 88 active trials testing liposomal bupivacaine (Exparel) as of March 2021. Eight of these trials are co-sponsored by Pacira. Forty-three of those trials have primary completion dates in the next year (March 2021 through March 2022). Although there are often greater lags between primary completion and data publication for IGTs than industry-funded trials, we should still expect to see a significant number of readouts over the next year. Each readout is potentially more fuel for Heron's marketing campaign.

Exparel Ongoing Trials Part 1 of 2

NCT Number	Title	Start Date	Primary Completion Date	Completion Date
NCT04751344	Liposomal Bupivacaine Versus Bupivacaine Plain for Operative Pain Management of Forefoot Surgery	16-Jun-20	Jun-22	Jun-22
NCT03737604	TAP Blocks With Ropivacaine Continuous Infusion Catheters vs Single Dose Liposomal Bupivacaine After Kidney Transplant	4-Oct-18	1-Jun-21	1-Oct-21
NCT04066296	Outcomes for Lumbar Decompressions With Use of Liposomal Bupivacaine	Sep-21	Dec-21	Jan-22
NCT03922620	Liposomal Bupivacaine vs Peripheral Nerve Block	23-Jan-20	Jan-21	Jan-21
NCT04479371	Liposomal Bupivacaine vs Standard Penile Block for Hypospadias Repair	Jul-21	30-Jul-22	30-Jul-23
NCT04461028	Liposomal Bupivacaine in Shoulder Arthroscopy	21-May-19	21-May-21	21-May-22
NCT04539730	Liposomal Bupivacaine in Adductor Canal Blocks (ACB)	1-Aug-21	1-Oct-21	1-Oct-21
NCT03907033	Liposomal Bupivacaine in Vaginal Hysterectomy	3-Sep-19	31-Dec-21	31-Dec-21
NCT03906617	Bupivacaine/Epinephrine +Dexamethasone vs. Liposomal Bupivacaine	10-Apr-19	10-Apr-20	10-Jun-20
NCT03738696	Liposomal Bupivacaine in Rotator Cuff Repair	15-Dec-19	1-Dec-20	1-Dec-20
NCT04047446	Liposomal Bupivacaine vs Dexamethasone ISB	11-Jul-19	27-Aug-21	27-Aug-22
NCT04180943	Liposomal Bupivacaine Versus Bupivacaine for Postoperative Pain Control in Shoulder Surgery	13-Dec-19	1-Dec-21	1-Mar-22
NCT02749968	Intercostal Liposomal Bupivacaine for the Management of Blunt Chest Wall Trauma	9-Mar-18	Jan-21	Jan-21
NCT04382144	Levobupivacaine Versus Liposomal Bupivacaine (Exparel®) for Treatment of Pain and Disability in Lateral Epicondylitis	1-Sep-20	31-Dec-21	1-May-22
	Liposomal Bupivacaine and Intrathecal Hydromorphone for Women With Gynecological Malignancies Undergoing			
NCT04258631	Laparotomy	9-Jul-20	31-Jan-22	31-Mar-22
NCT03745040	Liposomal Bupivacaine in One-level Instrumented Posterior Spinal Fusion	26-Jan-19	Jan-22	May-22
NCT04333095	Sternal Block With Liposomal Bupivacaine vs. Saline Prior to Incision in Cardiac Surgery	6-Feb-20	Jun-21	Jun-21
NCT04571606	Interscalene Catheter vs. Interscalene Liposomal Bupivacaine for Arthroscopic Rotator Cuff Repair	14-Oct-20	Mar-21	Mar-21
NCT04117074	Thoracic Epidural Analgesia vs Surgical Site Infiltration With Liposomal Bupivacaine Following Open Gynecologic Surgery	Mar-21	Mar-23	Mar-24
NCT03305666	Trial of Injected Liposomal Bupivacaine vs Bupivacaine Infusion After Surgical Stabilization of Rib Fractures	5-Oct-17	20-Jul-20	31-Dec-20
NCT03599635	Pec Infiltration With Liposomal Bupivacaine for Breast Surgery	1-Jul-18	Dec-20	Dec-20
NCT03854344	Liposomal Bupivacaine Versus Lidocaine for Skin Graft Donor Site Pain	18-Mar-19	31-Dec-20	31-Dec-20
NCT04254692	Optimizing Recovery in Abdominoplasty	5-Jan-21	Jun-22	Jun-23
NCT04003506	Effectiveness of Adductor Canal Block Using Liposomal Bupivacaine	Dec-20	Oct-21	Oct-21
NCT04685421	Liposomal Bupivacaine Pharmacokinetic Study After Median Sternotomy Incision Infiltration in a Pediatric Cardiac Surgery	6-Jan-21	6-Jan-22	6-Jan-23
NCT02805504	Liposomal Bupivacaine for Postoperative Pain Control in Urologic Procedures	Jun-16	Dec-22	Jun-23
NCT03080142	TAP Block Catheters vs Liposomal Bupivacaine for Pain Control After Colorectal Surgery	1-Mar-17	1-Jul-19	16-Dec-20
NCT03638960	Interscalene Single Shot With Plain Bupivacaine Versus Liposomal Bupivacaine for Arthroscopic Shoulder Surgery	21-Feb-19	Mar-21	Jun-21
NCT04393207	TAP Block Using Liposomal Bupivacaine for Post-cesarean Delivery Analgesia- Walking Towards Recovery	1-Aug-20	30-May-21	30-Aug-21
NCT04360421	Use of Long-acting Bupivacaine In Lower Extremity Amputation	1-May-20	1-Feb-21	1-Feb-21
NCT03664986	Pudendal Block Using Liposomal Bupivacaine vs. Standard Treatment During Sacrospinous Ligament Fixation	24-Sep-18	1-May-21	1-May-21
NCT03929146	Liposomal Bupivacaine Versus Interscalene Nerve Block	5-Feb-19	1-Dec-21	1-Dec-21
NCT04644796	A Randomized Trial of Exparel vs Saline in Opioid Reduction of Pain Management Following Lumbar Spine Surgeries.	Apr-21	Jan-23	Jan-24
NCT04603911	RCT Comparing ESPB Solutions in Breast Surgery	4-Dec-20	May-21	May-21
NCT03702621	Comparing Liposomal Bupivacaine VS Standard Bupivacaine in Colorectal Surgery	30-Aug-18	31-Dec-20	Aug-21
NCT04272086	Utility of Liposomal Bupivacaine Transversus Abdominal Plane Block for Open Myomectomy	9-Nov-20	Dec-22	Dec-22
NCT03574376	Liposomal Bupivacaine Intercostal Nerve Block vs Thoracic Epidural for Regional Analgesia in Multiple Rib Fractures	29-Aug-18	1-Aug-20	1-Aug-21
NCT03587584	Liposome Bupivacaine in Interscalene Block for Rotator Cuff Repair	16-Jul-18	1-Sep-20	1-Sep-20
NCT04585867	Liposomal Bupivacaine vs Bupivacaine for Pain Control After Sternotomy	11-Oct-17	10-Oct-23	10-Oct-23
NCT04047745	Post-operative Exparel Study Following Rotator Cuff Repair	Sep-19	Sep-21	Sep-21
NCT04005859	Pain Control in Colorectal Surgery: Liposomal Bupivacaine Block Versus Intravenous Lidocaine	22-Feb-18	22-Feb-20	22-Feb-20
NCT03731221	Pectoral Fascial Plane and Serratus Anterior Plane Blocks With Bupivacaine v. Liposomal Bupivacaine	1-Nov-18	Dec-22	Dec-22
	Repeat or Single Quadratus Lumborum Block for the Reduction of Opioid Prescriptions After Surgery in Retropertitoneal			
NCT04189783	Sarcoma Patients ("RESQU-SARC" Trial)	8-Jun-20	31-Dec-21	31-Dec-21
NCT04611958	Intraductal Liposomal Bupivacaine for Chronic Pancreatitis	1-Apr-21	31-Dec-21	31-May-22

Source: Cowen and Company, ClinicalTrials.gov

Exparel Ongoing Trials Part 2 of 2

NCT Number	Title	Start Date	Primary Completion Date	Completion Date
NCT04074226	ESP vs QL for Total Abdominal Hysterectomy	Mar-21	Dec-22	Dec-22
NCT04777591	Effectiveness of Exparel TAP Block in Breast Free Flap Reconstruction	10-Mar-21	28-Feb-23	28-Feb-24
	Thoracic Epidural Analgesia Versus Rectus Sheath Block Versus Surgeon Infiltration With Liposomal Bupivacaine or			
NCT04300231	Standard Bupivacaine for Post-Operative Pain Control After Cystectomy	22-Oct-19	May-21	May-22
NCT04559347	Local Anesthetic as Single Shot Versus Catheter in Patients Undergoing Video Assisted Thoracoscopic Surgery	10-Dec-20	Dec-21	Dec-22
NCT04685876	Comparing Bupivacaine, and Placebo for Plane Blocks	Mar-21	Dec-22	Jul-23
NCT03975283	Use of Exparel for Postoperative Analgesia Following Bariatric Surgery	Aug-19	Aug-21	Aug-21
NCT03730402	Laparoscopic Assisted Plane Block (LAPB) Trial	4-Feb-19	Sep-20	Feb-21
NCT04209504	Evaluating Hemidiaphragmatic Paralysis With Prolonged Neural Blockade From an Interscalene Brachial Plexus Block	22-Oct-20	1-Aug-21	2-Aug-21
NCT03870685	Surgical Site Infiltration of Exparel vs TAP Block With Exparel in Patients Undergoing Laparotomy Via Midline Incision	5-Jul-18	31-Jul-21	31-Dec-21
NCT03682224	Exparel and Marcaine for Pain Management in Thoracoscopic Lobectomy Patients	5-Jul-18	5-Jul-23	5-Dec-23
NCT04382859	TOTEM: Trial of TAP Block Effective Medications	1-Dec-20	Dec-20	Feb-21
NCT03326180	Study of Peri-Articular Anaesthetic for Replacement of the Knee	29-Mar-18	Feb-21	Aug-21
	Comparing Local Anesthetics for Transversus Abdominis Plane (TAP) Block During Abdominally-based Free Flap for Breast			
NCT03700970	Reconstruction	13-Jun-19	15-Mar-21	30-Jun-21
	A Study to Analyze the Effects of Exparel for Post-Surgery Pain Control in Patients Undergoing Penile Prosthesis			
NCT04801368	Placement	1-Apr-21	1-Apr-23	1-May-23
NCT03587636	Liposome Bupivacaine Interscalene Total Shoulder	17-Jul-18	Oct-20	Dec-20
NCT04121338	Temporary Celiac Ganglion Block as a Test Before Celiac Ganglion Resection for Dysautonomia-Related Bowel Dysmotility	9-Dec-19	1-Oct-21	1-Oct-21
NCT03504865	Post-Mastectomy Analgesia Using Exparel (Liposomal) Versus Standard Bupivacaine or Placebo	1-Jul-19	Dec-20	Dec-21
NCT03636542	Evaluation of Diaphragm Movement After an Interscalene Block	1-Aug-18	Oct-21	Oct-21
NCT03859635	Erector Spinae Block Versus Surgeon Infiltration in VATS Procedures	7-Feb-19	30-Jun-21	30-Aug-21
NCT03927326	Postoperative Analgesia in Laparoscopic Abdominal Surgery After Exparel Via TAP or Local Infiltration	Aug-19	Jul-20	Jul-20
NCT03827291	QL Block With Exparel in Colectomy	31-Oct-19	1-Apr-21	8-Apr-21
NCT04764916	Evaluation of Exparel Adductor Canal Field Block for Pain Control After ACL Reconstruction	16-Feb-21	16-Feb-22	2-Mar-22
NCT03496610	Surgeon Infiltration QL Block Comparison	25-Jan-21	1-Dec-21	1-Dec-21
NCT03377595	Post C-Section Pain Control Using EXPAREL	2-Jul-19	30-Jun-20	1-Sep-20
	Efficacy of Laparoscopic-assisted Transversus Abdominus Plane (TAP) Block Compared to Ultrasound-guided TAP Block in			
NCT04345341	Minimally Invasive Gynecologic Surgeries: A Prospective, Randomized Control Trial.	Oct-20	May-21	Jun-21
NCT04781075	Modified TAP (Transverse Abdominis Plane) Block in Colorectal Surgery	1-Dec-17	31-Dec-20	31-Jul-21
NCT04655339	Laparoscopic Transversus Abdominis Plane (TAP) Block to Reduce Post-operative Opioids	10-Dec-20	1-Jul-24	1-Jul-24
NCT03743194	Pectoralis and Serratus Muscle Blocks	1-Dec-18	Dec-22	Dec-22
NCT03187379	Efficacy of Exparel (TM) on Post-operative Pain After Laparoscopic Gastric Bypass Using Circular EEA Stapler	1-Jun-17	1-Jul-21	1-Jul-21
NCT03827213	Exparel Interscalene vs Indwelling Catheter	22-Jan-19	29-Sep-21	29-Sep-21
NCT03541941	Exparel vs. Bupivacaine Hydrochloride vs. Placebo for Hernia Repair	3-Jul-18	Jun-21	Dec-21
NCT04003987	ESP Block VS TAP in Laparoscopic Hysterectomy	1-May-19	Apr-21	Apr-24
NCT03420638	EXPAREL Post-tonsillectomy Clinical Trial	15-Feb-18	1-Jul-20	31-Dec-20
NCT04415931	Local Infiltration Analgesia Vs. Interscalene Block in Total Shoulder Arthroplasty	15-Aug-20	15-Jul-23	15-Jul-24
	Thoracic Epidural Analgesia or Four-Quadrant Transversus Abdominus Plane Block in Reducing Pain in Patients			
NCT03214510	Undergoing Liver Surgery	4-Oct-17	31-Aug-22	31-Aug-23
NCT03739021	Exparel for Total Shoulder Pain	Nov-19	1-Mar-20	15-Nov-20
NCT04046068	Multimodal Perioperative Pain Management: ComfortSafe Program	11-May-20	Jul-21	Sep-21
NCT04549090	Ultrasound Guided Posterior Quadratus Lumborum Block for Postoperative Analgesia in Gynecologic Surgery	1-Oct-20	31-Dec-21	31-Dec-21
NCT03867539	Exparel and Education to Avoid Opioids After Carpal Tunnel Release	15-Feb-19	31-Jan-21	31-Jan-21
NCT04364867	Exparel for Total Shoulder Arthroplasty	1-Jun-20	1-Jun-23	1-Dec-23
NCT04421196	Opioid-free Total Hip Arthroplasty	1-Jul-21	1-Dec-21	1-Dec-21
	Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of EXPAREL, EXPAREL Admixed With Bupivacaine HCl vs. Bupivacaine HCl Administered as Combined Sciatic and Saphenous Nerve Blocks for Postsurgical Analgesia in Subjects			
NCT04518462	Undergoing Lower Extremity Surgeries	20-Oct-20	16-Mar-21	1-Apr-21
NCT03972397	Intercostal Nerve Cryoablation for Postoperative Pain Management	1-Aug-19	1-Aug-20	1-Aug-20
NCT04504812	A Sequenced Strategy for Improving Outcomes in People With Knee Osteoarthritis Pain	1-Feb-21	Aug-24	Sep-24

Source: Cowen and Company, ClinicalTrials.gov

Pacira P&L

FY ending Dec 31st in \$000s, except per share amount	2020A	1QE	2QE	3QE	4QE	2021E	2022E	2023E	2024E	2025E	2026E
Revenues:											
EXPAREL	413,338	114,690	119,676	129,649	134,636	498,650	532,710	547,799	563,613	587,687	611,457
iovera	8,817	2,976	2,738	3,559	2,631	11,903	15,474	19,342	23,211	26,692	29,362
Other Product Sales	4,459	375	345	345	435	1,500	1,500	1,500	1,500	1,500	1,500
Total net product sales	426,614	118,040	122,759	133,553	137,701	512,053	549,684	568,641	588,324	615,879	642,319
Collaborative licensing and milestone revenue	0	0	0	2,230	3,344	5,574	20,167	19,463	31,824	48,185	77,578
Royalty revenue	3,033	773	712	726	883	3,094	3,156	3,219	3,283	3,349	3,416
Total revenues	429,647	118,814	123,470	136,508	141,928	520,721	573,006	591,322	623,430	667,413	723,312
Operating expenses:											
Cost of goods sold	117,328	30,723	28,265	29,878	34,026	122,893	129,906	128,312	128,560	130,404	140,100
<i>Gross margin</i>	73%					76%	77%	78%	79%	80%	80%
Research and development	59,421	16,341	15,034	15,334	18,655	65,363	66,670	68,004	69,364	70,751	72,166
Selling, general and administrative	193,516	58,055	53,410	57,683	63,071	232,219	250,797	270,860	292,529	315,932	341,206
Product discontinuation	5,166										
Amort. of acquired intangible	7,866	2,000	2,000	2,000	2,000	8,000	8,000	8,000	8,000	8,000	8,000
Total operating expenses	383,297	107,119	98,709	104,896	117,751	428,475	447,373	475,177	498,453	525,086	561,473
Income (loss) from operations	46,350	11,695	24,761	31,613	24,177	92,246	125,633	116,146	124,977	142,327	161,840
Other (expense) income:											
Interest income	4,629	1,169	1,169	1,169	1,169	4,675	4,722	4,769	4,817	4,865	4,914
Interest expense	(25,671)	(5,776)	(5,776)	(5,776)	(5,776)	(23,104)	(20,794)	(18,714)	(16,843)	(15,158)	(13,643)
Loss on early extinguishment of debt	(8,071)					0	0	0	0	0	0
Royalty interest obligation	0					0	0	0	0	0	0
Other, net	2,852	(500)	(500)	(500)	(500)	(2,000)	100	101	102	103	104
Total other expense, net	(26,261)	(5,107)	(5,107)	(5,107)	(5,107)	(20,429)	(15,971)	(13,844)	(11,924)	(10,190)	(8,625)
Income (loss) before income taxes	20,089	6,588	19,654	26,505	19,070	71,817	109,661	102,302	113,053	132,136	153,215
Income tax (expense) benefit	125,434	(3,232)	(3,232)	(3,232)	(3,232)	(12,927)	(19,739)	(18,414)	(21,480)	(25,106)	(30,643)
GAAP Net income (loss)	145,523	3,356	16,422	23,274	15,838	58,890	89,922	83,888	91,573	107,030	122,572
Total adjustments	(48,954)	14,716	14,716	14,716	14,716	58,866	48,809	50,849	52,992	55,242	57,604
Non-GAAP Net income (loss)	96,569	18,072	31,139	37,990	30,555	117,756	138,731	134,737	144,565	162,272	180,175
Net income (loss) per share:											
GAAP Net income (loss) per common share	3.33	0.08	0.37	0.53	0.36	1.34	1.99	1.82	1.94	2.23	2.50
Non-GAAP Net income (loss) per common share	2.21	0.41	0.71	0.86	0.69	2.68	3.07	2.92	3.07	3.37	3.67

Source: Cowen and Company

Ticker	Rating	Price*	Price Target	Ticker	Rating	Price*	Price Target
HRTX	Outperform	\$16.59	\$34.00	PCRX	Market Perform	\$69.99	\$54.00

*As of 04/01/2021

VALUATION METHODOLOGY AND RISKS

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

April 6, 2021

ADDENDUM**Stocks Mentioned In Important Disclosures**

Ticker	Company Name
HRTX	Heron
PCRX	Pacira BioSciences

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The recommendation contained in this report was produced at April 05, 2021, 16:40 ET. and disseminated at April 06, 2021, 06:00 ET.

April 6, 2021

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Assumption: The expected total return calculation includes anticipated dividend yield

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	540	68.18%	176	32.59%
Hold (b)	243	30.68%	22	9.05%
Sell (c)	9	1.14%	0	0.00%

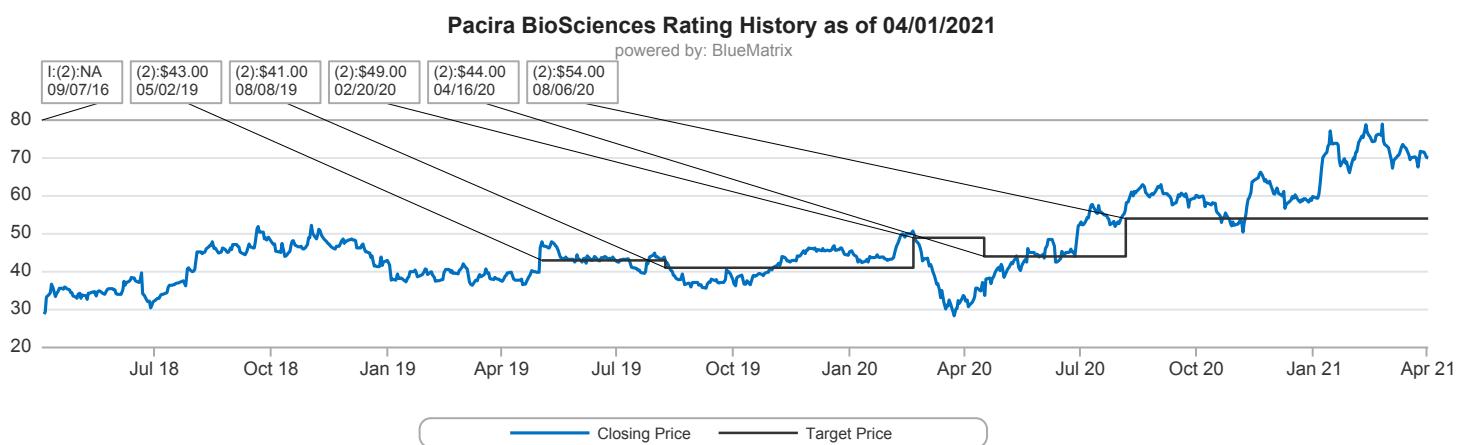
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Heron Rating History as of 04/01/2021

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